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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,593	06/21/2001	Daniel E. Afar	G&C 129.18USD1	9040

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AGENSYS C/O MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE, SUITE 500
SAN DIEGO, CA 92130

EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,593	AFAR ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-91* is/are pending in the application.

4a) Of the above claim(s) *73-79 and 81-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72,80,90 and 91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Election filed August 4, 2003 (Paper No. 12) in response to the Office Action of May 14, 2003 is acknowledged and has been entered.

Claims 72-91 are pending.

Claims 73-79, and 81-89 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 72, 80, and 90-91 are currently under prosecution

Applicant's election with traverse of Group I, claim 72 in Paper No 12 is acknowledged. Applicants argue that the language of Claim 72 makes no limitations to being practiced "in-vitro" as delineated in the restriction requirement. Applicants further submit (page 9) that Claims 72 and 80 are related as subcombination to a combination because claim 80 is clearly directed to a combination while claim 72 is clearly directed to the corresponding subcombination of methods involving administration of an altering composition. In this regard, applicants assert that restriction was improper between Groups I and VI. This argument has been considered and is found persuasive. The restriction requirement between Groups I and VI is now vacated such that Claims 72, 80, and 90-91 are one Group. However, with regards to applicant's assertion that Groups I and IV are "genus" claims (page 8), such arguments are only persuasive to the extent that claims 90 and 91 are species. Therefore, the inventions encompassing the methods of Groups II-V (Claims 73-79) and the methods of Groups VII-XII (Claims 81-89) remain

independent and or distinct for the reasons set forth in Paper No. 10. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification

The specification is objected to for the following reason: The specification on page 1 should be amended to reflect the current priority status of the present application, for example:

This application is a divisional of US patent application 09/374,135, filed August 10, 1999, now U.S. Patent No. 6,277,972, etc.

The brief description of Figure 9 (page 6) is objected to because the figure does not appear to show BPC-1 mRNA expression in "a bladder carcinoma" cell line. Also, see page 9, line 21; page 25, line 25; and page 41, line 11. The latter indicates that lane 15 (cell line 5637) showed expression, but lane 15 appears clear. Clarification is requested.

The specification is further objected to on page **37**, line 30 and page **42** for improper disclosure of nucleic acid sequences without a respective sequence identifier, i.e. a SEQ ID NOs:. Hence, the disclosure fails to comply with the requirements of 37 CFR 1.821 through 1.825. In the absence of a sequence identifier for each sequence, Applicant must provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where

applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d). *Failure to supply the appropriate sequences identification numbers in response to this action will be considered non-responsive.*

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 72, 80, and 90-91 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As a first matter, the word "modulating" is unclear. How is a cell which is to be modulated distinguished from a cell which is not modulated? Secondly, it is not clear what is included or excluded by an "altering" composition. In what way is the composition distinguished between one that alters and one that does not alter? Lastly, Claim 80 is indefinite for reciting "treating" as it not clear what is being treating. If the subject is to receive some treatment effect, there must be some reference as to what is being treating to observe said effect. Hence the metes and bound of the claimed method cannot be determined.

Claims 72, 80, and 90-91 are further rejected as vague and indefinite for reciting the term 19P1E8 as the sole means of identifying the expressed gene referred to in Claims 72 and 80. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. This rejection can be obviated by amending the claims to specifically and uniquely identify 19P1E8, for example, by SEQ ID NO.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 72, 80, and 90-91 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the *claimed* invention. A search of applicant's disclosure did not reveal a **method of modulating** cells that express 19P1E8 comprising administering to the cells that express 19P1E8 an **altering composition**, whereby the composition **alters the status** of 19P1E8 or **alters the status of a molecule** that is modulated by 19P1E8. Further, claimed limitations to ex-vivo and or in vivo were inconsistent with the teachings of the specification. Hence, this is a new matter rejection. Applicants are reminded that with respect to newly added or amended claims, applicants should show support in the original disclosure for the new or amended claims. See MPEP §714.02 and § 2163.06.

If applicant should disagree with this rejection, applicant should submit evidence pointing to the serial number, page and line where support can be found for the disputed terminology.

Claims 72, 80, and 90-91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the

invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method of "modulating" cells either ex-vivo or in-vivo and or a method of treating a subject comprising administration of an "altering" composition which alters the status of an expressed gene (referred to as "19P1E8") or alters the status of a molecule that is modulated by the gene whereby the cells which express 19P1E8 are modulated.

Due to the indefiniteness of the claim language (see 112, 2nd above) it is assumed for examination purposes that the claims encompass inhibiting the growth of cancer cells (either ex-vivo or in-vivo) by the addition of a composition which interacts with the expression of 19P1E8. For example, see page 31, lines 1-5.

The specification teaches that *normal* expression of 19P1E8 mRNA is limited to the adult and fetal brain but is predominately expressed in prostate cancer xenografts and to some extent, albeit questionable, may be expressed in a bladder cancer cell line (see objection to Figure 9 above). The specification further proposes (page 10, line 23) that 19P1E8 is directly involved in oncogenesis because it shows transforming activity in soft agar assays and binds to a cellular protein expressed by cells including those expressing 19P1E8 (BPC-1).

However, notwithstanding the above teachings, the claims are not enabled because the specification provides insufficient guidance and or objective evidence to predictably enable one skilled in the art to make and use an "altering" composition that would effectively treat a subject and or modulate the status of cells that express 19P1E8 (i.e. inhibit the growth of said cells and

or provoke apoptosis of said cells), including modulation of said cells ex-vivo and or in-vivo. The fact that a protein may be expressed in prostate cancer (to the exclusion of other normal tissues) or that its expression has oncogenic potential does not lend reasonable guidance to one of skill in the art to make and or use any and all potentially altering compositions against said expressed protein which may or may not provoke some type of modulation of the gene. For example, even when certain genes have a confirmed oncogenic status, the ability to modulate said gene in-vitro does not extrapolate to the same effects in-vivo. Indeed, Gaiger *et al.* (Blood, Volume 96, No. 4, August 2000, pages 1480-1489) chose to evaluate the Wilm's tumor antigen (WT1) as a potential immunotherapeutic as it is well known in the art that WT1 protein expression is more abundant in leukemia cells than in normal hematopoietic ells. (Similarly, the specification proposes cancer vaccines comprising a BPC-1 composition-page 32.) However, WT1 peptide immunization did not show any effect on tumor growth in-vivo (Figure 10, page 1486).

In addition to the general observations above, the specification fails to objectively demonstrate **(either in-vitro, ex-vivo, or in-vivo)** *any* treatment of subjects and or modulation of cells that express 19P1E8 by the administration of any "altering composition". Hence, the specification fails to provide a reasonable nexus between the claimed modulation or targeting of 19P1E8 and any observable effect (or therapeutic effect such as the treatment of cancer) such as the inhibition of cell growth in cells that express 19P1E8. Furthermore, since no nexus has been shown, it would require undue experimentation for one of ordinary skill in the art to make, use, and or screen for the thousands of potentially "altering" compositions in any predictable manner.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable for one skilled in the art to make and use the method as broadly claimed. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 72, 80, and 91 are rejected under 35 U.S.C. 102(e) as being anticipated by Coffey *et al.* (US Patent No. 6,030,793, February 9, 1993).

US Patent No. 6030793 teaches methods of modulating the status of cells expressing BPC-1 (i.e. 19P1E8) by administering an altering composition whereby the composition alters the status of 19P1E8 whereby cells that express 19P1E8 are modulated, including in-vivo modulation (column 2, lines 37-61; column 13, lines 22-54). The patent further teaches a method of treating a subject which method comprises cells that express 19P1E8 by modulating said cells comprising administering to the cells in vivo an altering composition, whereby the composition alters the status of 19P1E8 whereby cells that express 19P1E8 are modulated and the subject receives some treatment effect (column 18, lines 57+).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
October 15, 2003

Gary B Nickol